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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/424,521 02/15/00 NIELSEN

P ISIS-3070

HM22/0227

EXAMINER

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ART UNIT	PAPER NUMBER
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1635

DATE MAILED:

02/27/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/424,521	NIELSEN ET AL.
	Examiner Thomas G. Larson, Ph.D.	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 November 2000.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 15-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 15-52 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892)
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 18) Interview Summary (PTO-413) Paper No(s) _____.
- 19) Notice of Informal Patent Application (PTO-152)
- 20) Other: _____

1. The following action is responsive to Applicant's request for reconsideration in the paper filed 11/06/00 with a certificate of mailing dated 11/02/00.
2. Receipt of the sequence listing in computer readable format (CRF) on 11/06/00 is acknowledged. The CRF disk has been processed and the CRF has been found to be proper.
3. The amendment to the continuing data filed 11/06/00 is objected to because it does not provide the relationship between each application and the prior application of which it claims benefit. The continuing data should state whether each application is a national phase filing, continuation, continuation-in-part, divisional, etc, of the application of which it claims benefit. See MPEP § 201.11 (under "Reference to First Application") for example.
4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
5. Claims 15-17, 25, 26, and 31 stand rejected under 35 U.S.C. 102(b) as being anticipated by Thomson et al. (WO 93/12129, designated "AQ" on the Information

Disclosure Statement filed 3/17/00) for the reasons set forth in the Office action mailed 8/02/00.

Applicant's arguments filed 11/06/00 have been fully considered but they are not persuasive. Applicant traverses the rejection essentially on the grounds that the '765, 387, and '363 parent applications disclose certain species that support the breadth of the current generic claims.

Applicant is correct in asserting that the '387 and '363 applications disclose lipids and steroids as terminal groups, which are lipophilic species. However, it is not clear that recitation of the two species lipids and steroids, are necessarily representative of the broad genus of lipophilic compounds. For example bridged cycloalkanes, such as the adamantoyl group recited in claims 19, 22, 30 and 37, and shown on Fig. 1 of the instant disclosure, and the heptyl-succinyl and palmytyl-succinyl groups, also shown in Fig. 1, do not appear to be contemplated in the '387 and '363 disclosures. The narrow disclosure of only two species that are clearly lipophilic does not attest to the fact that applicant had conceived of the terminus as being a generic lipophilic group, and, therefore, does not appear to support the priority claim to a generic lipophilic group.

Applicant further argues that the examiner has relied on the same species disclosed in the Thomson document as disclosed in applicant's priority documents to reject the claims. In reply, it is submitted that while it only requires disclosure of a single species to anticipate a genus under 35 USC 102 (MPEP 2131.02), more is

required to support the possession of a genus (note MPEP 2163.02 and 2163.05(I), for example). Furthermore, the Examiner did not rely solely on the same features, as asserted by applicant. As specifically pointed out in the Office action mailed 8/2/00, Thomson et al. specifically teach at p. 6, lns. 3-6, that the terminal group may be a lipophilic group ("...Q may function to increase lipophilicity ...").

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 15-18, 25-27, and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over (WO 93/12129, designated "AQ" on the Information Disclosure Statement filed 3/17/00) for the reasons set forth in the Office action mailed 8/02/00.

Applicant's arguments filed 11/06/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thompson et al. is not available as prior art. However, Thompson et al. is available as prior art for the reasons set forth in the rejection of claims 15-17, 25, 26 and 31 under 35 USC 102(b).

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8. Claims 15-18, 25-27 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson et al. as applied to claims 15-18, 25-27, and 31 above, and further in view of Buchardt et al. (WO 92/20702), designated "AO" on the Information Disclosure Statement filed 3/17/00) for the reasons set forth in the

Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

9. Claims 15, 19, 25, and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over either Thomson et al. alone or in combination with Buchardt et al. (WO 92/20702) as applied to claim 15 and 25 above, and further in view of Haas et al. for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

10. Claims 15, 19, and 25-30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over either Thomson et al. alone or in combination with Buchardt et

al. (WO 92/20702) and taken in view of Haas et al. as applied to claim 15, 19, 25 and 30 above, and further in view of Lansdorp (WO 97/14026) for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

11. Claims 15-18, 20-22, 25-27, 31-34, and 38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over either Thomson et al. alone or in combination with Buchardt et al. (WO 92/20702) as applied to claims 15-18, 25-27, and 31 above, and further in view of Buchardt et al. (TIBTECH) for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

12. Claims 15, 19-22, 25, 30, 32, and 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson et al. either alone or in combination with Buchardt et al. (WO 92/20702) and in view of Haas et al. as applied to claims 15,

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19, 25, and 30 above, and further in view of Buchardt et al. (TIBTECH) for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

13. Claims 25, 28, 29, 32, 35, and 36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over either Thomson et al. alone or in combination Buchardt et al. (WO 92/20702) and taken in view of Haas et al, and further in view of Lansdorp (WO 97/14026) as applied to claims 15, 19, 25, 28, and 29 above, and further in view of Buchardt et al. (TIBTECH) for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. Applicant traverses the rejection solely on the grounds that Thomson et al. is not available as prior art. However, Thomson et al. is available as prior art for the reasons set forth previously in this office action.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 23, 24, and 39-52 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the Office action mailed 8/2/00.

Applicant's arguments filed 11/6/00 have been fully considered but they are not persuasive. A *prima facie* case of undue experimentation was established based on the analysis set forth in *In re Wands* (8 USPQ2d 1400) in the Office action mailed 8/2/00. While applicant alleges that the rejection does not provide sufficient grounds to doubt that the present claims are enabled, it is submitted that it is well established that claims are not enabled when it would require undue experimentation for the skilled artisan to make and/or use the invention (MPEP 2164.01). It is also accepted that the analysis set forth in *In re Wands* provides a method for determining whether or not undue experimentation is required to make and/or use a claimed invention (MPEP 2164.01(a)). In this case the evidence as a whole was weighed (MPEP 2164.05) and the it was found that the preponderance of the evidence clearly favored a finding of undue experimentation.

Applicant argues that they are "under no obligation to" provide the teachings required to overcome the obstacles known in the art to the effective therapeutic application of peptide nuclei c acids. However, it is clear that the obstacles in the

art to the effective therapeutic application of the invention are precisely those obstacles which require undue experimentation to solve to enable the therapeutic application of the claimed invention. For example, a peptide nucleic acid can not be used as an effective therapeutic if it can not be effectively delivered to its site of action. If applicant does not disclose or teach how to overcome such problems without engaging in undue experimentation, then the disclosure does not enable claims drawn to therapeutic embodiments.

Applicant alleges that insufficient evidence was provided to support a finding of lack of enablement. However, it is noted that four publications discussing the state of the art (Gewirtz, Rojanasakul, Hyrup, and Buchardt) were presented. It is noted that applicant has not provided any evidence to rebut the teaching of these disclosures. Applicant further alleges that the rejection fails to consider the entirety of the teachings of these documents and cites passages from Rojanasakul and from Gewirtz to rebut the finding of lack of enablement. Applicant states that the Rojanasakul reference "...states that compounds such as those recited in the claims show great promise" and cites Rojanasakul as teaching that "...it is expected that in the future these ON drugs will be commonly used...." However, a disclosure must be enabling at the time it is filed (MPEP 2164.05(a)). While an expectation of future success may speak to utility, it does not allow the artisan to solve the impediments to practicing the claimed invention at the time it was made without engaging in undue experimentation. Similarly, in the quote from the introduction

to the Gewirtz publication, the use of the qualifier "apparent" in the phrase "...apparent ... ease of use..." suggests that it appears as such but is not necessarily so. Indeed, Gewirtz devotes a substantial portion of the publication to detailing why the compounds are not easily used.

Applicant is correct that working examples are not required to enable a claimed invention. However, the absence of working examples that correlate with the claimed invention are a consideration in making a determination of undue experimentation in the analysis se forth in *Wands* (MPEP 2164.01(a)), particularly in an unpredictable or undeveloped art (MPEP 2164.02). In this case the finding of undue experimentation was not based solely on the absence of working examples, but was based on the totality of the available evidence.

It is noted that applicant has mainly addressed the aspects of the rejection relating to the state of the art and the absence of working examples in the *Wands* analysis. It is noted that applicant's response remains silent with regard to the other factors considered in the analysis such as the breadth of the claims, the predictability of the art and the nature and amount of experimentation required to practice the claimed invention. It is also noted that applicant has made no evidence of record to rebut the teachings of Buchardt, Gewirtz, Hyrup, and Rojanasakul which were used to establish the undeveloped and unpredictable state of the art. Thus, applicant's arguments are not found convincing and the rejection is maintained.

16. U.S. Patent No. 5,773,571 to Nielson et al. is made of record as having been cited in applicant's response but not having been previously made of record.

17. No claim is allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The FAX numbers are (703) 308-4242 and (703) 308-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the

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original copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Unofficial papers, such as draft responses, may be transmitted to the examiner directly at (703) 305-7939. It is recommended that the examiner be notified when a fax is sent to this number.

Any inquiry concerning this communication or earlier communications should be directed to Thom Larson, whose telephone number is (703) 308-7309. The examiner normally can be reached Monday through Friday from 9:00 AM to 5:30 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

Thomas G. Larson, Ph.D.
Examiner

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600